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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,819	04/26/2005	Keiichi Kawai	Q87268	9379

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EXAMINER	
HAMIDINIA, SHAWN A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 05/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/532,819	KAWAI ET AL.	
	Examiner	Art Unit	
	Shawn Hamidinia	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *11-17,19 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 18 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1-10, 18 and 20, drawn to a method for determining the binding site with plasma protein of a first drug.

Group II, claims 11-17, drawn to a method for detecting mutation of plasma protein.

Group III, claims 19 and 21, drawn to a kit for carrying out the method of Group II.

2. Upon thorough consideration of the claims, the examiner has determined that a lack of unity of invention exists, as defined in Rule 13.

PCT Rule 13.2 states that unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. Annex B, Part 1(b), indicates that "special technical features" means those technical features which as a whole define a contribution over the prior art. In the instant case, the method of Group I for determining the binding site with plasma protein is entirely different than the method

of Group II for detecting mutation of plasma protein. Since each method does not have a common special technical feature, Groups I-III lack unity.

3. Applicants' election without traverse of Group I in the telephonic interview on May 10, 2006 is acknowledged. Claims 11-17, 19 and 21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected groups.

Priority

4. The current application filed on April 26, 2005 is a 371 of PCT/JP03/13572 filed on October 23, 2003 which claims benefit to Japanese application 2002-317568 filed on October 31, 2002.

Information Disclosure Statement

5. The information disclosure statement filed on April 26, 2005 has been considered. Please see the attached initialed PTO-1449.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-10, 18 and 20 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 7-8 of U.S. Patent No. 7,029,653. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application are directed to a method for determining the binding site with plasma protein of a first drug by reacting the first drug for which the binding site with plasma protein is to be determined with a second drug of which the binding site with plasma protein is known, then determining the change in the ratio of the first drug freed due to the binding of the plasma protein with the second drug. This is obvious in light of the claims from US Pat. 7,029,653 which are directed to a method of in-vivo administration of drugs with binding affinity for plasma protein, where a first drug with binding affinity for plasma protein is added with a second drug, verapamil, which has binding affinity for the same plasma protein. In US Pat. 7,029,653, the method for determining the binding site occurs in-vivo, and wherein the first drug is labeled with a radioactive nuclide (US Pat. 7,029,653 claims 3-5). The

patent also includes a pharmaceutical preparation, wherein each of the first drug and the second drug is in a separate container, and prepared as a kit (US Pat. 7,029,653 claims 7-8).

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-10, 18 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawai et al. (WO 0078352) and Pritchard et al. (1985).

Note: I am relying on the English translation of the WO 0078352 application which is US Patent # 7,029,653.

Kawai et al. teach a method of administration of drugs with binding affinity for plasma protein and drugs regulating the effective ingredient does of drug with binding affinity for plasma protein, (see lines 8-11, column 1). Kawai et al. teach that when the second drug (such as bucolome, cefazolin, etoposide, verapamil, etc.) having high binding affinity for the same plasma protein, for which the first drug has binding affinity, is administered simultaneously or before administration of the first drug, then competitive displacement will take place at the binding site, so that the first drug may be released in a higher concentration, (see lines 31-37, column 3; lines 3-7, column 3).

Kawai et al. further teach that the second drug may be preferably selected from those having competitive binding affinity for the same plasma protein as the first drug; increasing the free fraction of the first drug by binding inhibition of the first drug with plasma protein; having the affinity for the same binding site of the first drug on plasma protein; and having the higher binding affinity for plasma protein, (see lines 50-59, column 3). Kawai et al. teach that additionally plural drugs may be used as the second drugs when a synergistic effect can be expected, (see lines 27-30, column 2; lines 54-55, column 4). Kawai showed the enhancement of the displacement effect by using plural second drugs together in experiments using 6-MNA and Verapamil added simultaneously, (see Example 6 and Table 10; lines 50-56, column 6).

Kawai et al. teach that the plasma protein used are human serum albumin (Has) and acid glycoprotein (AGP), (see lines 43-50, column 4). Kawai et al. also teach that the plasma protein is derived from human, (see example 1). Kawai et al. teach that the first drug is labeled with radioactive nuclides such as 99m-technetium, (see lines 43-54, column 2; Example 1). Kawai et al. further teach the method of the administration of drugs with binding affinity for plasma protein, wherein the radiodiagnostic drug for in vivo use or the radiotherapeutic drug for in vivo use is radiolabeled with one nuclide selected from the group consisting of 11-carbon, 15-oxygen, 18-fluorine, 32-phsophorus, 59-iron, 67-copper, 67-gallium-81m-krypton, 81-rubidium, 89-strontium, 90-yttrium, 99m-technetium, 111-indium, 123-iodine, 125-iodine, 131-iodine, 133-xenon, 117m-tin, 153-samarium, 186-rhenium, 188-rhenium, 201-thalium, 212-bismuth, 213-bismuth and 211-astatine, (see claim 5).

Kawai et al. further teach that the first drug and the second drug may be supplied as a kit form in which they are filled in a container separately (see lines 22-42, column 4). Kawai et al. also teach the use of ultrafiltration equipment, (see Examples, lines 19-24, column 7).

Pritchard et al. teach in vitro tests to investigate the plasma protein binding of bepridil using radiolabeled bepridil (Bepridil HCL-^{14}C). Pritchard et al. et al. teach the general procedure they employed to determine the effects of other drugs on the in vitro plasma protein binding of bepridil, (see paragraph 5-6, page 348). Pritchard et al. further teach the results of the in vitro tests at page 351, Table V. Pritchard et al. teach that the addition of verapamil, diltiazem and dsopyramide at ten- to 100-fold molar excess over bepridil resulted in significant displacement of bepridil from its plasma protein binding sites. The abstract of Pritchard et al. discloses that free fractions of bepridil were enhanced by addition of drugs such as (verapamil, nifedipine, diltiazem, disopyramide and warfarin).

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-10, 18 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Kawai et al. (US Pat. 7,029,653).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Conclusion

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawn Hamidinia whose telephone number is (571)

272-4534. The examiner can normally be reached on Mon-Fri from 9:00 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SAH

ROBERT A. WAX
PRIMARY EXAMINER